

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Kreutzer <i>et al.</i>	Art Unit	: 1635
Serial No.	: 10/612,179	Examiner	: Tracy Ann Vivlemore
Filed	: July 2, 2003	Conf. No.	: 5239
Title	: METHOD AND MEDICAMENT FOR INHIBITING THE EXPRESSION OF A GIVEN GENE		

MAIL STOP AMENDMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Applicants request consideration of the references listed on the attached PTO-1449 form. These references were cited in an opposition proceeding filed against a counterpart European patent. References A2 through A52 are submitted herewith. References A53 through A63 are submitted with a separate transmittal letter.

Non-patent references A19, A21, and A34 are in German. As required under 37 CFR § 1.98(a)(3), a concise explanation of the relevance of these documents is provided below. The statements below are essentially the same characterizations provided by the parties in the proceedings. English language translations of the documents are not readily available but can be obtained should the Examiner request them.

Reference A19: Dellweg *et al.*, ed., Römpf Lexikon Biotechnologie, p. 354 and p. 673 (1992) (in German);

This reference was cited by the patentee to introduce a definition of the term “hairpin” as a “Single stranded DNA- or (in vivo more frequently) RNA-sequences, which fold back onto themselves forming a loop structure, and which are stabilised by intramolecular interactions”.

This definition served to demonstrate that the double stranded RNA species exemplified in Example II of WO 00/44895 is not a hairpin as commonly understood despite the C18 linker, since it is not a continuous RNA strand. Hence, prior art demonstrating hairpins cannot anticipate such a structure.

Reference A21: Fallert-Müller, ed., Encyclopedia of Biochemistry, Vol. J-Z, pp. 448-449 (2000) (in German):

This reference was introduced by an opponent to provide a definition of the term "viroid" as the skilled person would read it.

Reference A34: Letter to the International Examining Authority from Gassner & Partner in the prosecution of PCT/DE00/00244 (WO 00/44895), 5 pages (March 28, 2001) (in German):

This reference was cited by an opponent. The letter states: "Double-stranded oligonucleotides having the complementary region of 25 or more successive nucleotides are known from post-published WO 99/32619."

This statement is being filed after a first Office Action on the merits, but before receipt of a final Office Action or a Notice of Allowance. Please apply the \$180 for payment of the late submission fee under 37 C.F.R. § 1.17(p) (and any other necessary charges or credits) to Deposit Account No. 06-1050, referencing Attorney Docket No. 14174-104US5.

Respectfully submitted,

Date: July 14, 2006

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Substitute Form PTO-1449 (Modified) Information Disclosure Statement by Applicant (Use several sheets if necessary) (37 CFR §1.98(b))	U.S. Department of Commerce Patent and Trademark Office		Attorney's Docket No. 14174-104US5	Application No. 10/612,179
	Applicant Kreutzer <i>et al.</i>			
	Filing Date July 2, 2003		Group Art Unit 1635	

U.S. Patent Documents							
Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	A1						

Foreign Patent Documents or Published Foreign Patent Applications								
Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Class	Subclass	Translation	
							Yes	No
	A2	DE 196 18 797	03/23/2000	Germany				X
	A3	DE 199 03 713.2	01/30/1999	Germany			X	
	A4	DE 199 56 568.6	11/24/1999	Germany			X	
	A5	EP 1 144 623 B1	08/28/2002	EPO			X	
	A6	EP 1 214 945	06/19/2002	EPO				X
	A7	EP 1 230 375 B1	07/06/2005	EPO				
	A8	WO 00/44495	08/03/2000	WIPO				

Other Documents (include Author, Title, Date, and Place of Publication)		
Examiner Initial	Desig. ID	Document
	A9	U.S. Provisional Patent Application No. 60/117,335, Li <i>et al.</i> (filed January 28, 1999)
	A10	U.S. Provisional Patent Application No. 60/130,377, Pachuk <i>et al.</i> (filed April 21, 1999)
	A11	Agrawal <i>et al.</i> , "Self-Stabilized Oligonucleotides as Novel Antisense Agents," <u>Delivery Strategies for Antisense Oligonucleotide Therapeutics</u> , Edited by Saghir Akhtar, CRC Press, pp. 105-121 (1995)
	A12	Barber <i>et al.</i> , "Mutants of the RNA-Dependent Protein Kinase (PKR) Lacking Double-Stranded RNA Binding Domain I Can Act as Transdominant Inhibitors and Induce Malignant Transformation," <i>Mol. Cell. Biol.</i> , 15(6):3138-3146 (1995)
	A13	Braich <i>et al.</i> , "Regiospecific Solid-Phase Synthesis of Branched Oligonucleotides. Effect of Vicinal 2',5'-(or 2',3'-) and 3',5'-Phosphodiester Linkages on the Formation of Hairpin DNA," <i>Bioconj. Chem.</i> , 8:370-377 (1997)
	A14	Brennicke <i>et al.</i> , "RNA editing," <i>FEMS Microbiology Reviews</i> , 23:297-316 (1999)
	A15	Byrom <i>et al.</i> , "Inducing RNAi with siRNA Cocktails Generated by RNase III," <i>TechNotes 10(1)</i> , Ambion, http://www.ambion.com/techlib/tn/101/4.html (2004)
	A16	Chien <i>et al.</i> , "Novel cationic cardiolipin analogue-based liposome for efficient DNA and small interfering RNA delivery <i>in vitro</i> and <i>in vivo</i> ," <i>Cancer Gene Therapy</i> , pp. 1-8 (2004)
	A17	Couzin, "Small RNAs Make Big Splash," <i>Science</i> , 298:2296-2297 (2002)
	A18	Czaderna <i>et al.</i> , "Structural variations and stabilizing modifications of synthetic siRNAs in mammalian cells," <i>Nucleic Acids Res.</i> , 31(11):1-12 (2003)

Examiner Signature	Date Considered
EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No. 14174-104US5	Application No. 10/612,179
Information Disclosure Statement by Applicant (Use several sheets if necessary)		Applicant <i>Kreutzer et al.</i>	
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(37 CFR §1.98(b))			

Other Documents (include Author, Title, Date, and Place of Publication)		
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	A19	Dellweg et al., ed., <u>Römpf Lexikon Biotechnologie</u> , p. 354 and p. 673 (1992) (in German)
	A20	Elbashir et al., "Analysis of gene function in somatic mammalian cells using small interfering RNAs," <i>Methods</i> , 26:199-213 (2002)
	A21	Fallert-Müller, ed., <u>Encyclopedia of Biochemistry</u> , Vol. J-Z, pp. 448-449 (2000) (in German)
	A22	Gryaznov et al., "Template controlled coupling and recombination of oligonucleotide blocks containing thiophosphoryl groups," <i>Nucleic Acids Res.</i> , 21(6):1403-1408 (1993)
	A23	Hedges, "The Origin and Evolution of Model Organisms," <i>Nature Reviews</i> , 3:838-849 (2002)
	A24	Hornung et al., "Sequence-specific potent induction of IFN- α by short interfering RNA in plasmacytoid dendritic cells through TLR7," <i>Nature Medicine</i> , 11(3):263-270 (2005)
	A25	Hu-Lieskovan et al., "Sequence-Specific Knockdown of EWS-FLI1 by Targeted, Nonviral Delivery of Small Interfering RNA Inhibits Tumor Growth in a Murine Model of Metastatic Ewing's Sarcoma" <i>Cancer Res.</i> , 65(19):8984-8992 (2005)
	A26	Hunter et al., "The characteristics of inhibition of protein synthesis by double stranded ribonucleic acid in reticulocyte lysates," <i>J. Biol. Chem.</i> , 250(2):409-417 (1975)
	A27	"InBase, The Intein Database: The Intein Registry – Inteins Sorted by Species," http://tools.neb.com/intbase/list.php (database updated on May 22, 2006)
	A28	International Preliminary Examination Report from PCT/DE00/00244
	A29	"Introduction of DNA into Mammalian Cells," <u>Current Protocols in Molecular Biology</u> , Supplement 48, Edited by Frederick M. Ausubel et al., John Wiley & Sons, Inc., pp. 9.4.7-9.4.8 (1999)
	A30	Judge et al., "Sequence-dependent stimulation of the mammalian innate immune response by synthetic siRNA," <i>Nat. Biotechnol.</i> , pp. 1-6 (2005) (8 pages of supplementary content included)
	A31	Kennerdell et al., "Use of dsRNA-Mediated Genetic Interference to Demonstrate that <i>frizzled</i> and <i>frizzled 2</i> Act in the Wingless Pathway," <i>Cell</i> , 95:1017-1026 (1998)
	A32	Kitabwalla et al., "RNA-Interference - A New Weapon Against HIV and Beyond," <i>N. Engl. J. Med.</i> , 347(17):1364-1367 (2002)
	A33	Lee et al., "The C. elegans Heterochronic Gene <i>lin-4</i> Encodes Small RNAs with Antisense Complementarity to <i>lin-14</i> ," <i>Cell</i> , 75:843-854 (1993)
	A34	Letter to the International Examining Authority from Gassner & Partner in the prosecution of PCT/DE00/00244 (WO 00/44895), 5 pages (March 28, 2001) (in German)
	A35	Marques et al., "Activation of the mammalian immune system by siRNAs," <i>Nat. Biotechnol.</i> , 23(11):1399-1405 (2005)
	A36	Martinez et al., "Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi," <i>Cell</i> , 110:563-574 (2002)
	A37	McManus et al., "Gene Silencing in Mammals by Small Interfering RNAs," <i>Nat. Rev. Genet.</i> , 3:737-747 (2002)
	A38	Moss et al., "The Cold Shock Domain Protein LIN-28 Controls Developmental Timing in C. elegans and Is Regulated by the <i>lin-4</i> RNA," <i>Cell</i> , 88:637-646 (1997)
	A39	Nielsen et al., "A novel class of conformationally restricted oligonucleotide analogues: synthesis of 2',3'-bridged monomers and RNA-selective hybridization," <i>Chem. Commun.</i> , pp. 825-826 (1997)
	A40	PCT/GB00/04404 as filed (November 19, 1999)

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	A41	Pegram <i>et al.</i> , "Phase II Study of Receptor-Enhanced Chemosensitivity Using Recombinant Humanized Anti-p185 ^{HER2/neu} Monoclonal Antibody Plus Cisplatin in Patients With HER2/ <i>neu</i> -Overexpressing Metastatic Breast Cancer Refractory to Chemotherapy Treatment," <i>J. Clin. Oncol.</i> , 16(8):2659-2671 (1998)
	A42	Perler, "InBase: the Intein Database," <i>Nucleic Acids Res.</i> , 30(1):383-384 (2002)
	A43	Regalado, "Turning Off Genes Sheds New Light On How They Work," <i>The Wall Street Journal</i> , 4 pages (August 6, 2002)
	A44	Robbins <i>et al.</i> , "Sensing the danger in RNA," <i>Nat. Med.</i> , 11(3):250-251 (2005)
	A45	Schwarz <i>et al.</i> , "Evidence that siRNAs Function as Guides, Not Primers, in the <i>Drosophila</i> and Human RNAi Pathways," <i>Mol. Cell</i> , 10:537-548 (2002)
	A46	Sharp <i>et al.</i> , "RNAi and double-strand RNA," <i>Genes Dev.</i> , 13:139-141 (1999)
	A47	Shi <i>et al.</i> , "A CBP/p300 homolog specifies multiple differentiation pathways in <i>Caenorhabditis elegans</i> ," <i>Genes Dev.</i> , 12:943-955 (1998)
	A48	Sinha, "Large-scale Synthesis. Approaches to Large-scale Synthesis of Oligodeoxynucleotides and their Analogs," <i>Antisense - From Technology to Therapy</i> , Volume 6, Edited by Reimar Schlingensiefen <i>et al.</i> , pp. 29-58 (1997)
	A49	Skripkin <i>et al.</i> , "Psoralen crosslinking between human immunodeficiency virus type 1 RNA and primer tRNA ₃ ^{Lys} ," <i>Nucleic Acids Res.</i> , 24(3):509-514 (1996)
	A50	Sledz <i>et al.</i> , "Activation of the interferon system by short-interfering RNAs," <i>Nat. Cell Biol.</i> , 5(9):834-839 (2003)
	A51	Soutschek <i>et al.</i> , "Therapeutic silencing of an endogenous gene by systemic administration of modified siRNAs," <i>Nature</i> , 432:173-178 (2004)
	A52	Strauss, "Candidate 'Gene Silencers' Found," <i>Science</i> , 286:886 (1999)
	A53	Timmons <i>et al.</i> , "Specific interference by ingested dsRNA," <i>Nature</i> , 395:854 (1998)
	A54	Tuschl <i>et al.</i> , "Targeted mRNA degradation by double-stranded RNA in vitro," <i>Genes Dev.</i> , 13:3191-3197 (1999)
	A55	Voinnet <i>et al.</i> , "Systemic signalling in gene silencing," <i>Nature</i> , 389:553 (1997)
	A56	Wargelius <i>et al.</i> , "Double-Stranded RNA Induces Specific Developmental Defects in Zebrafish Embryos," <i>Biochem. Biophys. Res. Commun.</i> , 263:156-161 (1999)
	A57	Waterhouse <i>et al.</i> , "Virus resistance and gene silencing in plants can be induced by simultaneous expression of sense and antisense RNA," <i>Proc. Natl. Acad. Sci. USA</i> , 95:13959-13964 (1998)
	A58	Wess <i>et al.</i> , "Early days for RNAi," <i>BioCentury</i> , 11(12):A1-A8 (2003)
	A59	Wianny <i>et al.</i> , "Specific interference with gene function by double-stranded RNA in early mouse development," <i>Nat. Cell Biol.</i> , 2:70-75 (2000)
	A60	Zamore <i>et al.</i> , "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals," <i>Cell</i> , 101:25-33 (2000)
	A61	Zeng <i>et al.</i> , "RNA interference in human cells is restricted to the cytoplasm," <i>RNA</i> , 8:855-860 (2002)

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	A62	Zhao <i>et al.</i> , "Double-Stranded RNA Injection Produces Nonspecific Defects in Zebrafish," <i>Dev. Biol.</i> , 229:215-223 (2001)
	A63	Zheng <i>et al.</i> , "Activation of the protein kinase PKR by short double-stranded RNAs with single-stranded tails," <i>RNA</i> , 10:1934-1945 (2004)

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